



Armed Forces College of Medicine

AFCM





Transplantation Immunology (1)

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- **By the end of this session the student will be able to:**
 - 1. Identify types of MHC antigens**
 - 2. Outline the pattern of inheritance in MHC molecules**
 - 3. Define types of grafts**
 - 4. Describe types of graft rejection**



Major Histocompatibility Ag (MHC) or Human leukocyte Antigen (HLA)



Are membrane glycoproteins expressed on **nucleated cells** & involved in **recognition of Ags by T lymphocytes**

Classes

There are 2 main classes : MHC class I & MHC class II

Site

MHC class I	MHC class II
All nucleated cells (including professional APCs)	Professional APC (MQ,DCs & B lymphocytes)



MHC Molecules



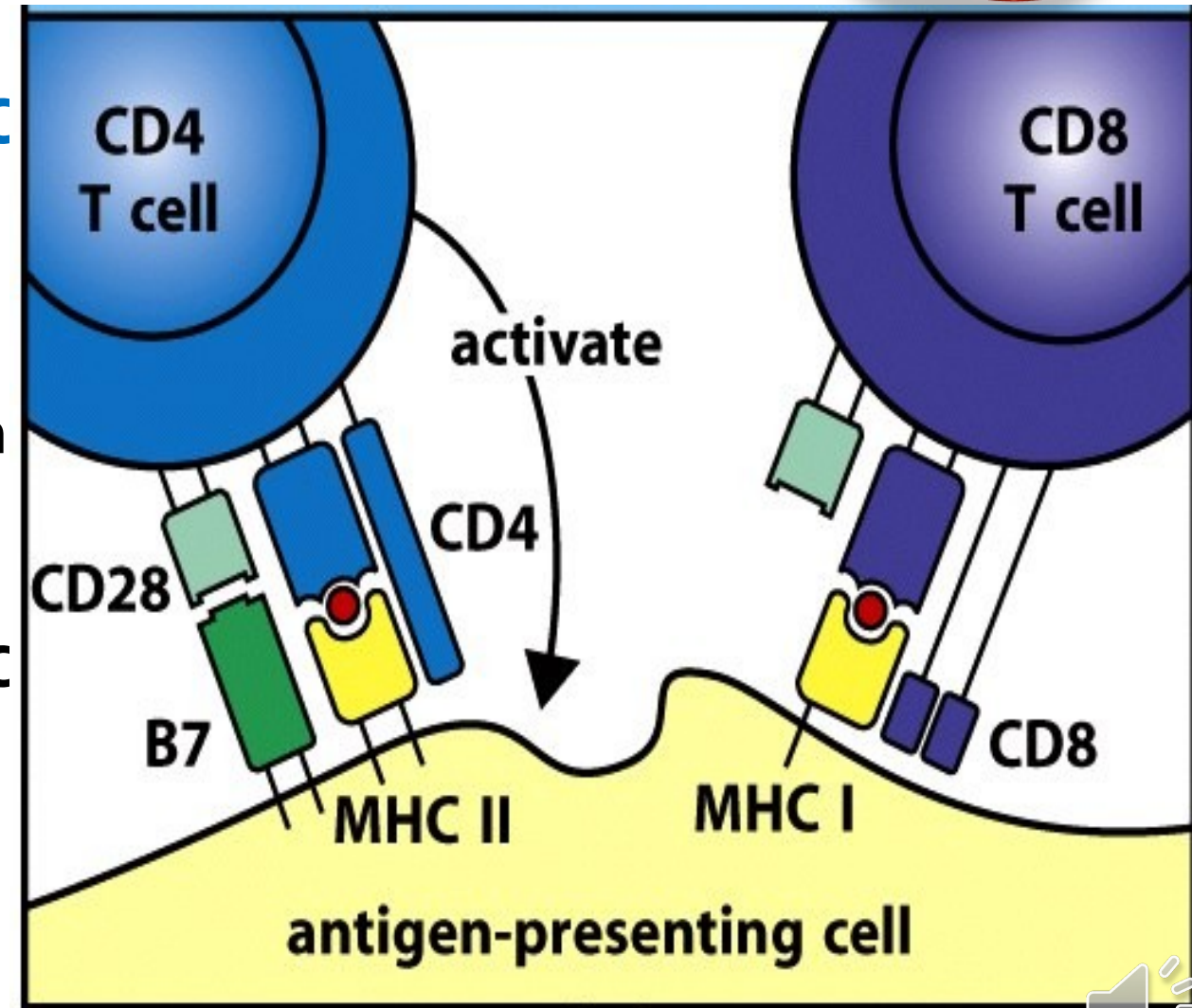
Importance

Ag recognition by T cells : MHC restriction

T lymphocyte recognize foreign peptide only in association with self MHC molecule :

- ✓ **Tc (CD8) cells** recognize MHC **class I** + peptide on the surface of APCs

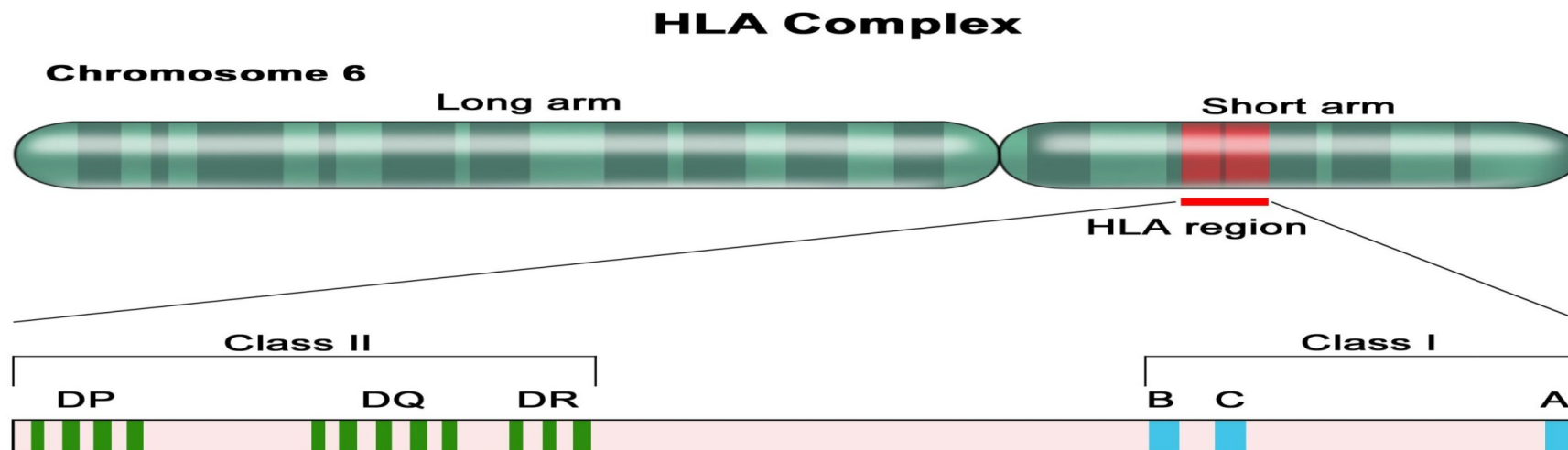
- ✓ **Th (CD4) cells** recognize MHC



Inheritance of MHC Molecules



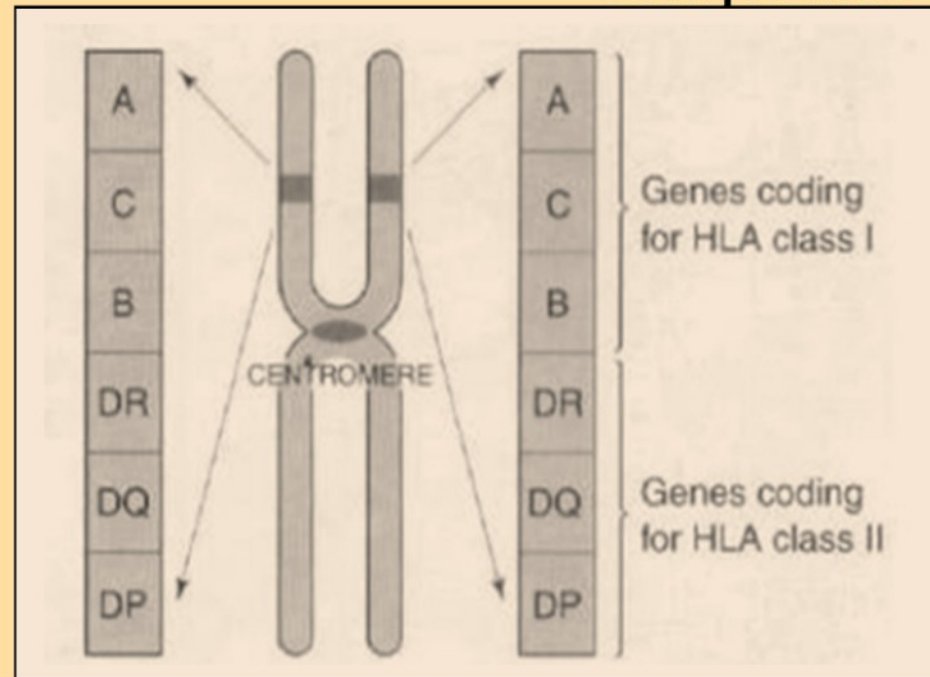
MHC Class I mol.	MHC Class II mol.
1- MHC proteins are coded by multiple genes on short arm of chromosome 6	
3 genes : A , C & B	3 genes : DR , DQ & DP
2-Each person has 2 sets of these genes : 1 paternal & 1 maternal	
3- Alleles inherited from both parents are co-dominantly expressed in each individual	
4-MHC genes are the most polymorphic genes in human genome	
A gene : 240 alleles B gene : 470 C gene : 110	DR gene : 350 alleles



In a nut shell ☺



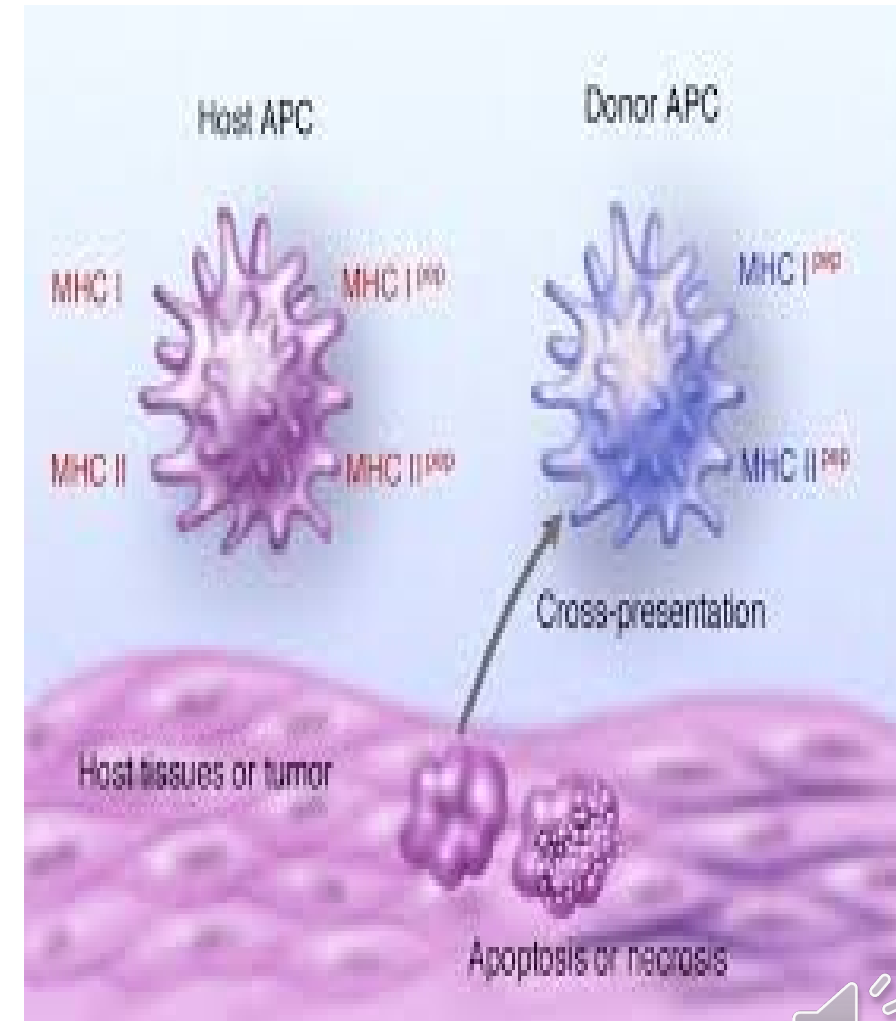
MHC genes are the **most polymorphic** genes in human genome → MHC proteins show **extensive polymorphism** in humans → Inevitable difference between donor & recipient → Donor MHC Ags are recognized *as foreign* by recipient IS



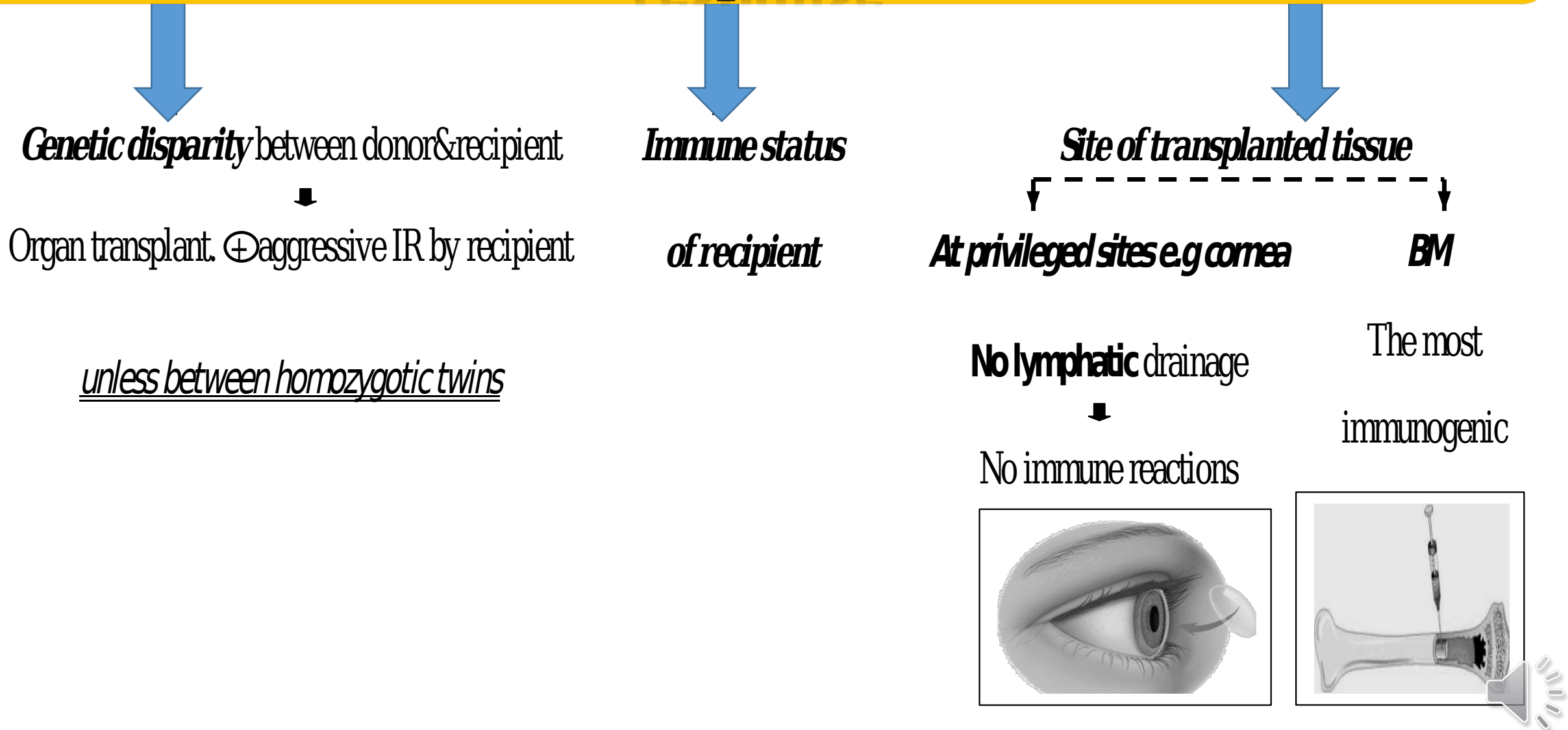
Role of MHC Molecules



- When T cells are exposed to foreign cells expressing non-self MHC, many clones are tricked into activation - their TCRs bind to foreign MHC-peptide complex's presented



Factors determining type & severity of Immune response



Types of Grafts

According to foreignness

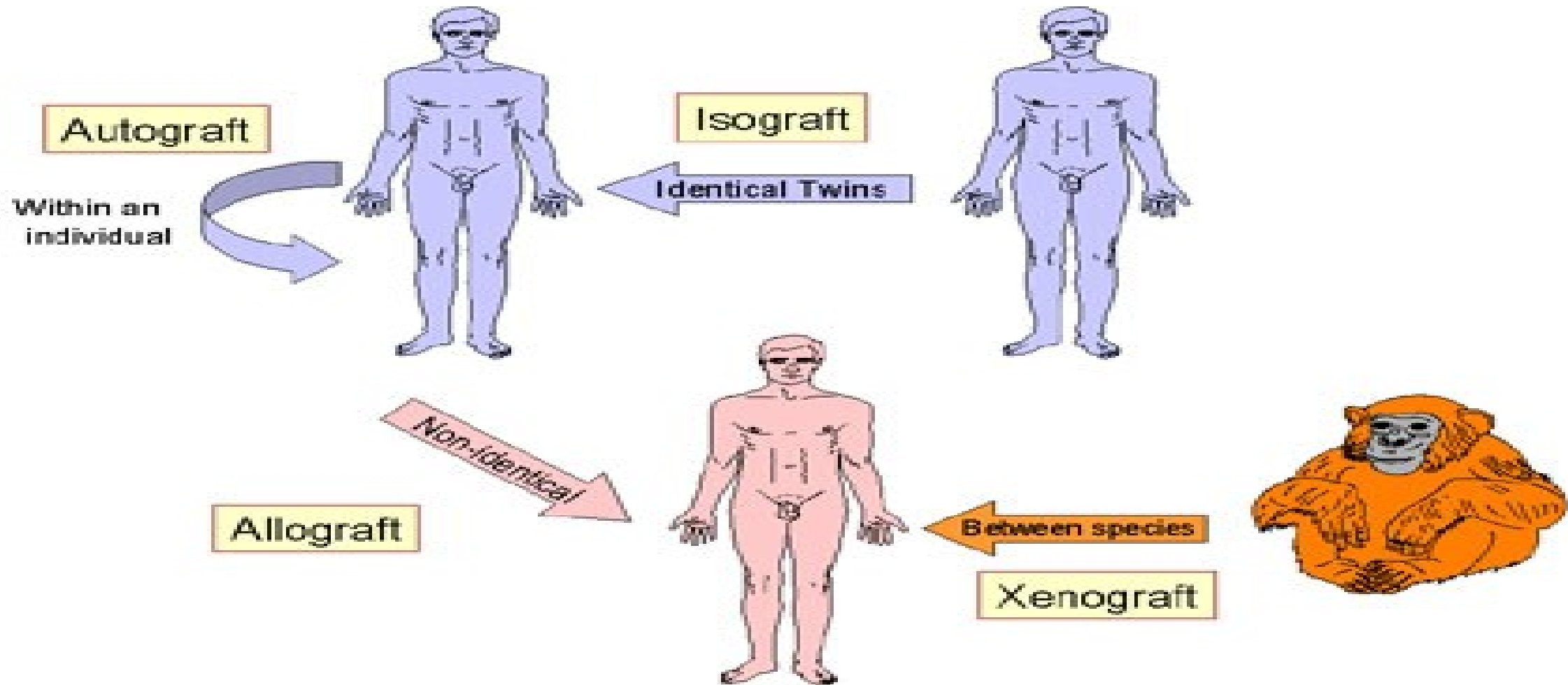


	Types	Immune rejection
1-Autograft	Graft from one area to another in the same individual (normal skin to a burned area)	NO, as the graft is autologus (self)
2-Syngraft (isograft)	Between identical twins	NO, as the 2 are histocompatible
3-Allograft (commnest type)	Between 2 genetically different individuals (allogenic) in the same species	YES , as the 2 are histoincompatible
4-Xenograft	Between a donor & recipient	





Types of Grafts





Types of Grafts

According to origin



From a living person
e.g. Kidney, BM



From a cadaver
e.g. heart,
lung,
cornea,



Types of Graft rejection



Acute

Commonest type

Time: 10 days
after
transplantation

Mechanism:
Activated T cells



Hyper acute

Time: Minutes

Mechanism: pre existing Ab
to Donor HLA Ag
OR
Mismatched ABO



Chronic

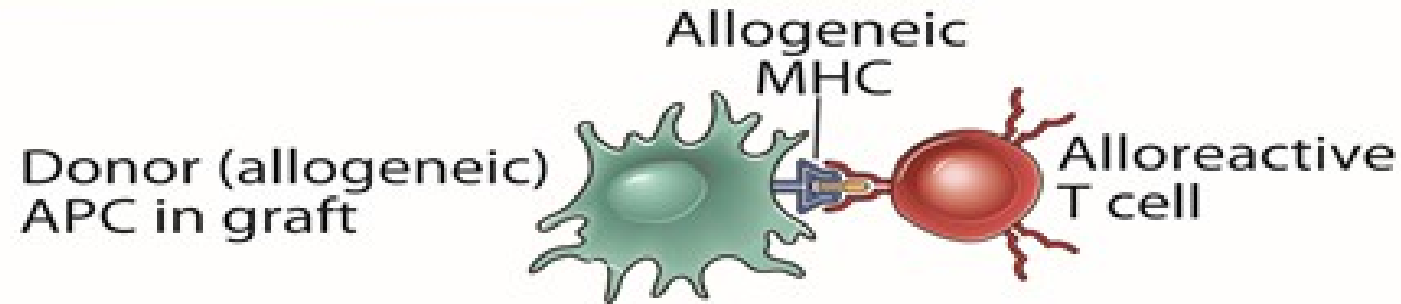
Time: Months

Mechanism:
i. Chronic delayed
hypersensitivity
of host lymph. to
alloAg in donor
vessel wall
ii. Repeated attacks
of acute rejection



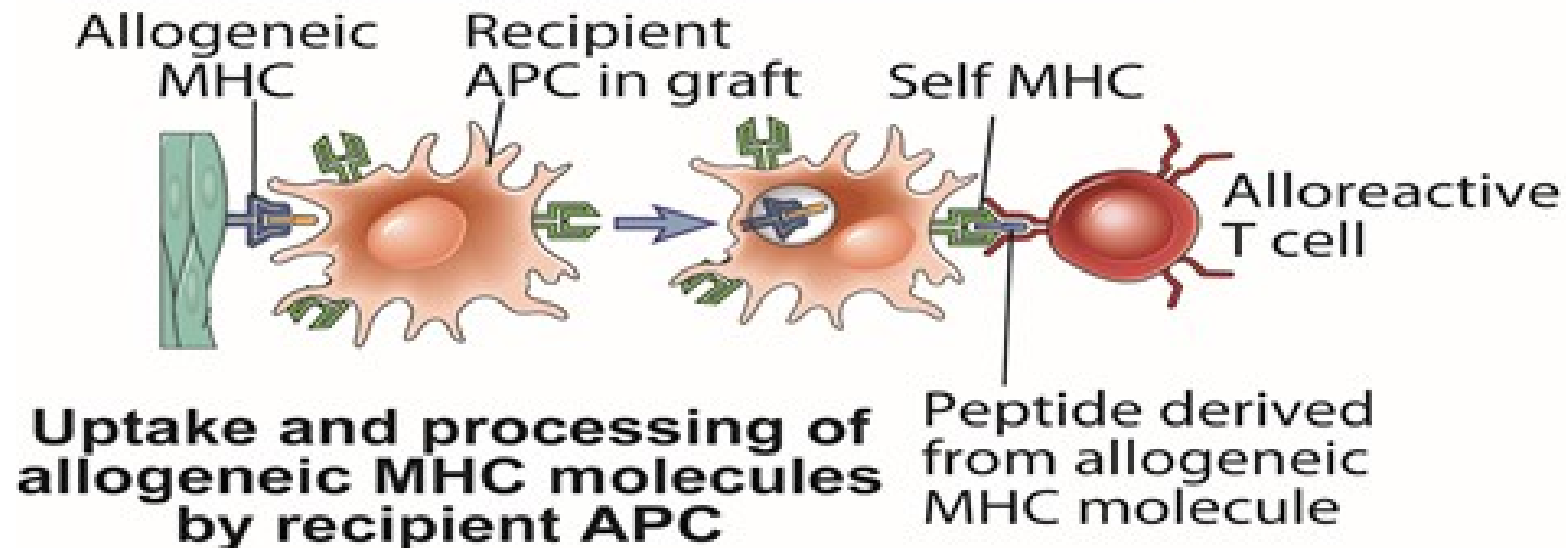
Mechanism of **ACUTE** Graft rejection

Direct alloantigen recognition



T cell recognizes unprocessed allogeneic MHC molecule on graft APC

Indirect alloantigen presentation



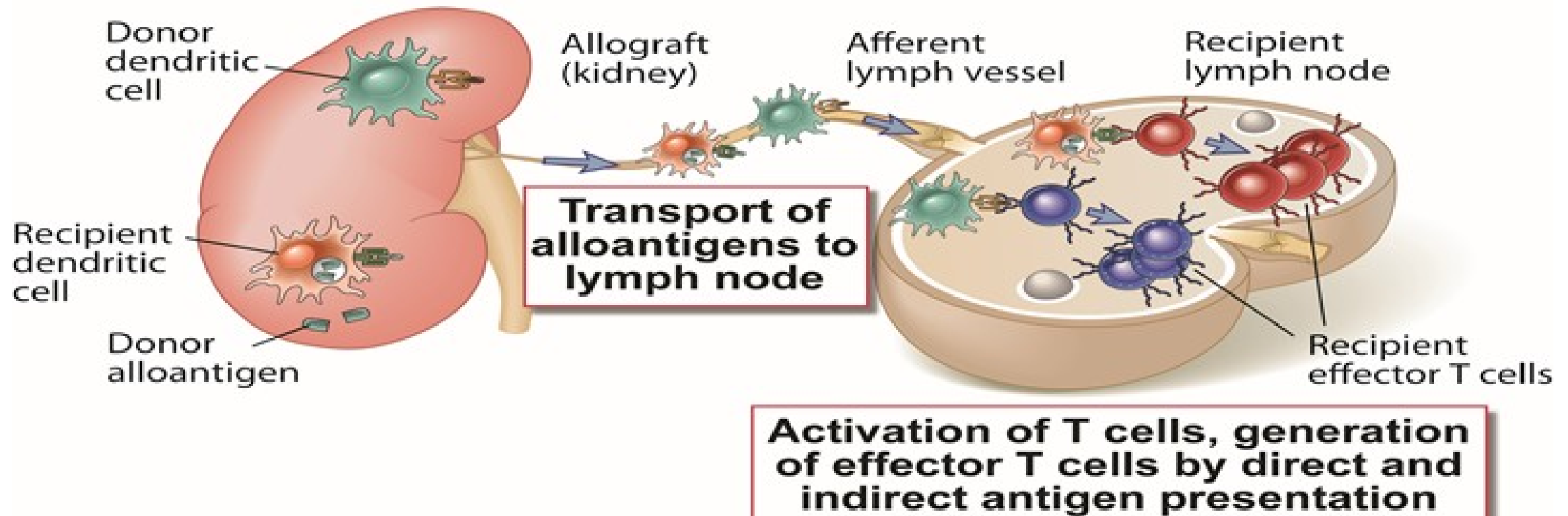
Presentation of processed peptide of allogeneic MHC molecule bound to self MHC molecule



Mechanism of **ACUTE** Graft rejection



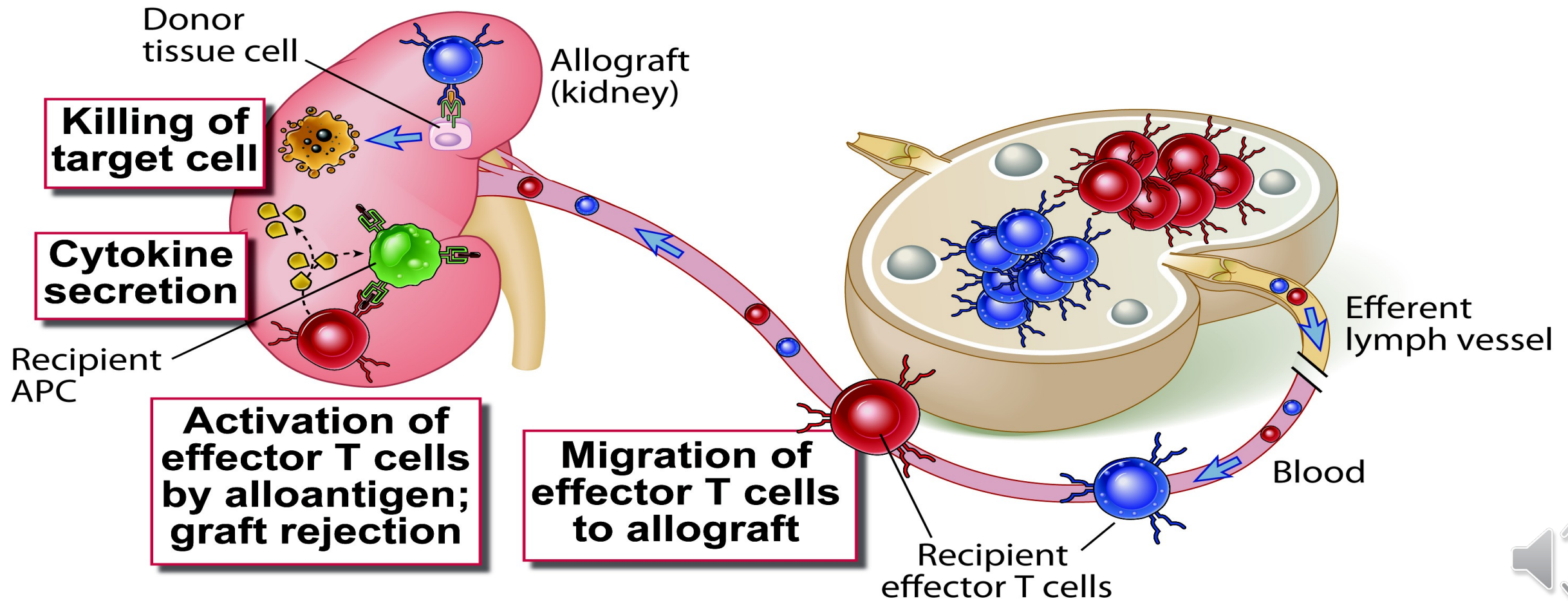
Sensitization



Destruction of allograft cells



Rejection



Destruction of allograft cells



C - Destruction of allograft cells

1-CD4 Th cells secrete cytokines → enhance graft damage

<u>IFNγ</u>	IL2
i. $\oplus$ CD8 Tc , MQ , NK & B cells to produce Abs	
ii. ↑ expression of allogenic MHC I & II on graft cells ↓ More vulnerable to CTLs & Abs	

2-CTLs (main effectors)

Attack graft cells & destroy them by direct cytotoxicity

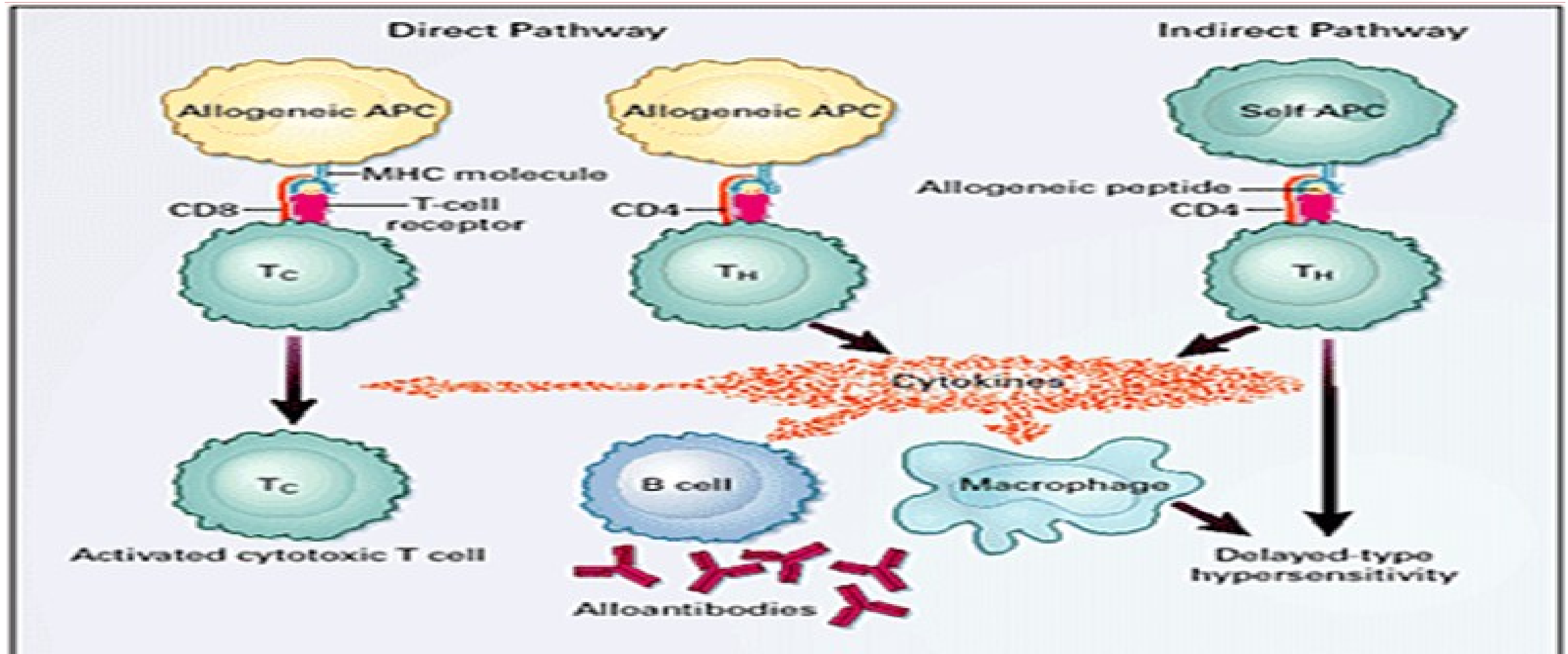
3-Ab damage graft by

↓
i. Complement activation

↓
ii. ADCC

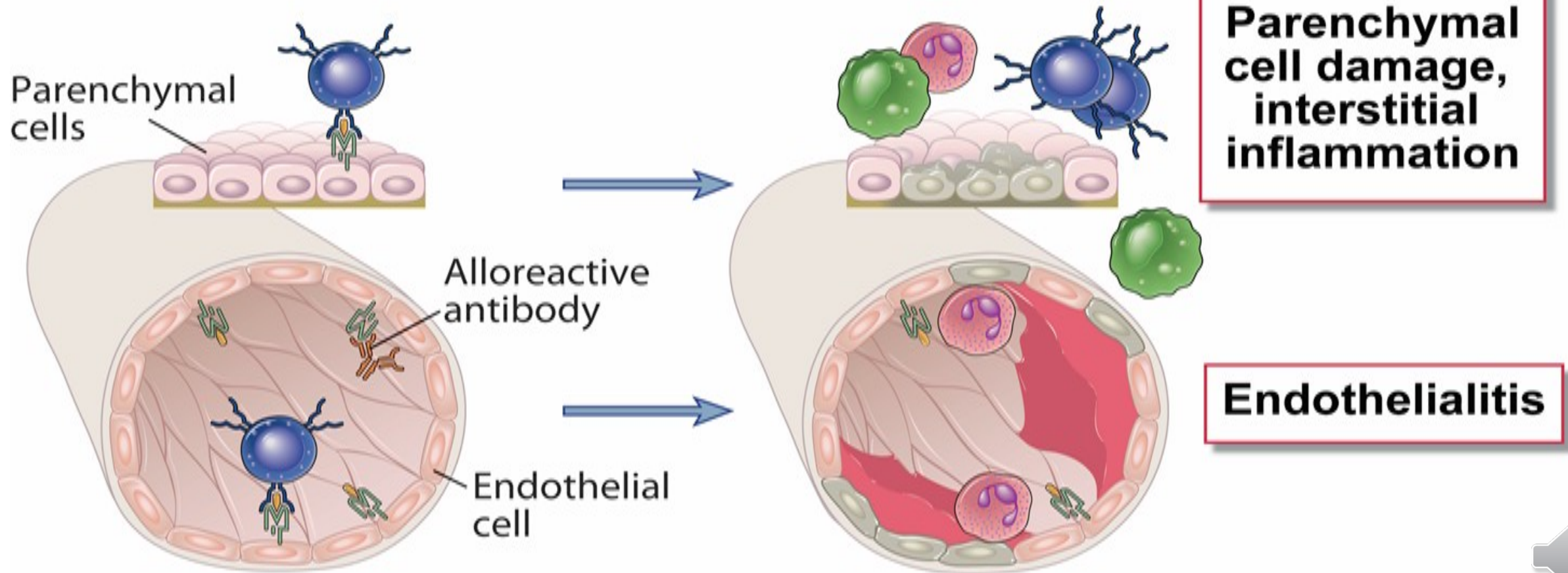


Destruction of allograft cells



Acute rejection

Acute rejection



Quiz



Regarding the MHC proteins and the genes that encode them, which one of the following is the most accurate?

(A) The genes encoding class II MHC proteins are highly polymorphic, whereas the genes encoding class I MHC proteins are not.

(B) The genes encoding class I MHC proteins are located on a different chromosome from the genes encoding class II MHC proteins.

(C) The genes are codominant, and each person expresses class I and class II MHC genes inherited from both mother and father.

(D) Class II MHC proteins are found on the surface of all



Suggested Textbooks



- 1. Review of Medical Microbiology and Immunology, Warren Levinson Chapter 62 p. 1150: 1162***
- 2. Cellular and molecular Immunology , Abul Abbas & Lichtmann, 2015, Chapter 117 p.359:382***



Thank
you

